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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/689,327	10/20/2003	Daniel J. Hassett	10738-51	2859

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EXAMINER	
ZEMAN, ROBERT A	
ART UNIT	**PAPER NUMBER**
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/689,327	HASSETT ET AL.	
	Examiner	Art Unit	
	Robert A. Zeman	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) *3-10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment and response filed on 5-22-2007 are acknowledged. Claim 1 has been amended. Claim 9 has been added.

Election/Restrictions

Newly submitted claims 9 and 10 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the elected invention is a method of Cystic Fibrosis disease assessment by detecting the presence or absence of a *Pseudomonas aeruginosa* outer membrane protein F (OprF), whereas newly added claim 9 is drawn to a method of Cystic Fibrosis disease assessment by detecting (determining) up-regulation of OprF (i.e. rise in mRNA levels) and claim 10 is drawn to a method of Cystic Fibrosis disease assessment by detecting antibodies to OprF.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 9 and 10 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Consequently, claims 1-10 are pending. Claims 3-10 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 1 and 2 are currently under examination.

Drawings

The objection to the drawings filed on 10-20-2003 is maintained for reasons of record. The reproductions of gels are still of such poor quality they were unreadable. New

corrected drawings are required in this application because due to the errors outlined above. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Claim Rejections Withdrawn

The rejection of claim 1 under 35 U.S.C. 102(b) as being anticipated by Mutharia et al. (Infection and Immunity, 1983, Vol. 42 No. 3, pages 1027-1033) is withdrawn in light of the amendment thereto. While Mutharia et al. disclose measuring OprF in *Pseudomonas aeruginosa* isolates from CF patients they do not disclose the limitation of the determining the anaerobicity of the patient's airway mucosal lining. It should be noted that this rejection might be reinstated upon the resolution of the new matter rejection set forth below.

The rejection of claims 1-2 under 35 U.S.C. 103(a) as being unpatentable over by Mutharia et al. (Infection and Immunity, 1983, Vol. 42 No. 3, pages 1027-1033) is withdrawn in light of the amendment thereto. Said reference does not disclose or render obvious the limitation of determining the anaerobicity of the patient's airway mucosal lining. It should be noted that this rejection might be reinstated upon the resolution of the new matter rejection set forth below.

Claim Rejections Maintained

35 USC § 112, Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1-2 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of detecting a *Pseudomonas aeruginosa* infection by the detection of its porin F protein (OprF), does not reasonably provide enablement for methods for assessing cystic fibrosis disease based on the presence or absence of any outer membrane protein generally, or OprF specifically; and the determination of whether a mucous lining in an airway of the individual is substantially anaerobic is maintained essentially for reasons of record. The specification still does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

Applicant argues:

1. The amendment to insert the identity of the particular infective agent, *Pseudomonas aeruginosa,* as the modifier/source of the OprF sufficiently restricts the breadth of the claim to what is enabled by the present specification and as set forth by the Examiner.

Applicant's arguments have been fully considered and deemed non-persuasive.

With regard to Point 1, contrary to Applicant's assertion, the amendment to the instant claims does not limit them to what is enabled by the instant specification. As set forth in the rejection the specification is enabling for methods of detecting a *Pseudomonas aeruginosa* infection by the detection of its porin F protein (OprF) but does not reasonably provide enablement for methods for assessing cystic fibrosis disease based on the presence or absence of any *Pseudomonas aeruginosa* outer membrane protein generally, or OprF specifically; and the determination of whether a mucous lining in an airway of the individual is substantially anaerobic. Additionally, the instant claims are

As outlined previously, enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary.

Nature of the invention: The instant claims are drawn to methods of assessing cystic fibrosis disease by detecting the presence or absence of outer membrane protein in a sample and determining whether a mucous lining in an airway of the individual is substantially anaerobic.

Breadth of the claims: The claims encompass the detection of the porin F protein of *Pseudomonas aeruginosa* and the mucous lining of any airway in an individual. Moreover, as the specification defines "assessment" as referring to the prognosis, monitoring, delaying progression, delaying early death, staging, predicting progression, predicting response to therapy regimen, tailoring of a therapy regimen, of Cystic Fibrosis disease based on the presence or absence of an outer membrane protein, the instant claims encompass the detection of any of the aforementioned proteins to achieve any of the aforementioned goals.

Guidance of the specification: The specification discloses that *Pseudomonas aeruginosa* infection is prevalent in CF patients and that OprF can be harvested from freshly excised lungs of CF patients. The specification further discloses that CF lung disease has been shown to dramatically worsen when *Pseudomonas aeruginosa* converts to the mucoid, alginate-overproducing form. Said conversion is coupled to the anaerobic growth of said bacteria and an increased production of OprF. Moreover, the specification discloses that the mucous lining of airways is anaerobic (especially in CF patients)[see page 11]. Finally, the specification defines "assessment" as referring to the prognosis, monitoring, delaying progression, delaying early

death, staging, predicting progression, predicting response to therapy regimen, tailoring of a therapy regimen, of Cystic Fibrosis disease based on the presence or absence of an outer membrane protein. However, the specification is silent on how said goals are to be accomplished using a single time point detection of a protein. Additionally, the specification is silent as to what role the "determination" of the anaerobicity of the mucous lining (which is disclosed in the specification as always being anaerobic) plays in said assessment.

State of the art: The art teaches that chronic *Pseudomonas aeruginosa* infection is associated with CF disease. The art further teaches that porin protein F (also known as OprF) is localized on the surface of the bacterial cell and is readily available for antibody binding (see Mutharia et al. Infection and Immunity, 1998, Vol. 42 No. 3, pages 1027-1033). Thus OprF is a good target for diagnostic methodologies. The art is silent with regard to any other *Pseudomonas aeruginosa* outer membrane proteins that have either a direct or indirect correlation with CF disease.

Consequently, due to the lack of guidance in art and in the specification, the claims are not enabled for the full breadth of the claims.

35 USC § 112, Written Description

The rejection of claims 1-2 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained for reasons of record. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention. This is a written description rejection.

Applicant argues:

1. The amendment makes it clear that the outer membrane protein recited in the instant claims is the porin protein F of *Pseudomonas aeruginosa.*

Applicant's arguments have been fully considered and deemed non-persuasive.

With regard to Point 1, contrary to Applicant's assertion, the instant claims are not limited to the porin protein F of *Pseudomonas aeruginosa.* Independent claim 1 recites the limitation "**a** *Pseudomonas aeruginosa* outer membrane protein". The use of the article "a" suggests that there is more than one outer membrane protein being claimed. Moreover, there is no recitation of the porin protein F of *Pseudomonas aeruginosa* aside from the confusing used of the abbreviation OprF (see rejection under 35 U.S.C. 112, second paragraph set forth below).

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, first paragraph "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The instant claims are drawn to methods of assessing cystic fibrosis disease by detecting the presence or absence of a *Pseudomonas aeruginosa* outer membrane protein in a sample, determining whether a mucous lining in an airway of the individual is substantially anaerobic wherein "assessing" is defined as referring to the prognosis, monitoring, delaying progression, delaying early death, staging, predicting progression, predicting response to therapy regimen,

tailoring of a therapy regimen, of Cystic Fibrosis disease based on the presence or absence of an outer membrane protein.

The instant claims all *Pseudomonas aeruginosa* outer membrane proteins whereas the specification only discloses the prevalence of *Pseudomonas aeruginosa* infections among CF patients and that OprF is readily found in CF patients with a *Pseudomonas aeruginosa* infection. The specification fails to describe any other *Pseudomonas aeruginosa* outer membrane protein that is either directly or indirectly associated with CF.

> Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)
> The skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404. 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and does so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams,

formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2datl966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claim 1-2 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the parenthetical use of the term "OprF" in claim 1 is maintained for reasons of record.

Applicant argues:

1. The amendment makes it clear that the outer membrane protein recited in the instant claims is the porin protein F of *Pseudomonas aeruginosa.*

Applicant's arguments have been fully considered and deemed non-persuasive.

With regard to Point 1, contrary to Applicant's assertion, the instant claims are not limited to the porin protein F of *Pseudomonas aeruginosa.* Independent claim 1 recites the

limitation "**a** *Pseudomonas aeruginosa* outer membrane protein". The use of the article "a" suggests that there is more than one outer membrane protein being claimed. Moreover, there is no recitation of the porin protein F of *Pseudomonas aeruginosa* prior to the recitation of the abbreviation "OprF".

It is unclear whether said term is meant to be an abbreviation for outer membrane proteins generally or is referring to the porin F protein of *Pseudomonas aeruginosa.* If the latter is the case it is unclear whether it is meant to be a limitation of the claim.

New Grounds of Rejection

35 USC § 112, New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicant has amended claim 1 to recite "making a determination of whether a mucous lining in an airway of the individual is substantially anaerobic, and (c) assessing the disease of the individual accordingly..." This phrase does not appear in the specification, or original claims as filed. The portion of the specification cited by Applicant as providing support for said

phrase is insufficient. Said portion of the specification (page 11, lines 6-16) merely is a disclosure of the fact that the mucous lining of airways is anaerobic (especially in CF patients). This disclosure does not provide support for the newly added method step wherein the anaerobicity of the mucous lining is determined. Therefore this limitation is new matter.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rendered vague and indefinite by the use of the term "substantially anaerobic". It is unclear what level of oxygen can be present wherein the mucous lining is still considered "substantially anaerobic" since said term is not explicitly defined in the specification.

Claim 1 is rendered vague and indefinite by the use of the phrase "assessing the disease of the individual accordingly". It is unclear on what said "assessment" is based. What are the criteria utilized? How is the result of the "determination" of step (b) utilized?. As written, it is impossible to determine the metes and bounds of the claimed invention.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (571) 272-0866. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov.

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ROBERT A. ZEMAN
PRIMARY EXAMINER
August 1, 2007